EXHIBIT B

VIRGINIA:

IN THE CIRCUIT COURT OF PRINCE WILLIAM COUNTY

SCOTT T. CARMINE, Plaintiff, v. GLEN JEFFREY POFFENBARGER, MD, *et al.* Defendants.	Case No. 15-5932

PLAINTIFF'S DESIGNATION OF EXPERT WITNESSES

COMES NOW, Plaintiff, by counsel, pursuant to Rule 4:1(b)(4) of the Supreme Court of Virginia and this Court's Scheduling Order, and identifies the following witnesses who may render expert testimony in the above-styled cause of action:

1. Eugene J. Carragee, MD
   Stanford University School of Medicine
   450 Broadway Street
   Pavilion C – MC 6342
   Redwood City, CA 94063

Dr. Eugene J. Carragee is a physician with expertise in the field of orthopedic surgery. His *curriculum vitae* is attached hereto as *Exhibit 1*.

Dr. Carragee is expected to testify, *inter alia*, in accordance with the contents of a medical article, of which he was lead author, entitled "A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned," published in The Spine Journal, accepted April 27, 2011, and attached hereto as *Exhibit 2*.

Dr. Carragee has reviewed the operative report of Defendant Dr. Glen Jeffrey Poffenbarger on his patient, Scott Carmine, on February 29, 2012, during which the patient underwent a "a left L3-5 TLIF" using Globus expandable PEEK cages into which Medtronic-supplied bone morphogenetic protein (BMP) had been placed, and each cage was inserted into the intervertebral spaces between L3-4 and L4-5. Additionally, Dr. Poffenbarger's operative report indicated that in addition to the PEEK cages at each level, "ADDITIONAL MORSELIZED BONE GRAFT WAS PLACED IN THE DISC SPACE AND TAMPED FORWARD. A BMP SPONGE WITH AUTOGRAFT WAS ALSO PLACED VENTRAL."

Dr. Carragee has also reviewed the October 14, 2013 operative report of Dr. Adam Crowl, which is attached hereto as *Exhibit 3*, and observed, *inter alia*, that there was incomplete fusion at L3-L4 and L4-L5 intervertebral spaces, and, more significantly, heterotopic bone both from the facet joint and interbody space of both L4-5 and L3-4 on the left side was "compressing the L3 root, traversing the L4 root, exiting L4 root, and traversing L5 root."

Dr. Carragee noted that prior to Dr. Crowl's surgery, the patient had given a history, following the surgery by Dr. Poffenbarger in 2012, that he had developed left leg pain after Dr. Poffenbarger's surgery which pain was initially in the left thigh, but had progressed down that leg to include both the L4 and L5 dermatomes, and, became so severe, that the patient required placement of a spinal cord stimulator for pain management. Following CT myelograms and an EMG (which demonstrated radiculopathy), it was determined that he had heterotopic ossification and a potential neoplastic lesion at L3-4 and L4-5 which had led to severe, unrelenting left leg pain with dysesthesias, hyperesthesias and left leg weakness. Advised of these findings, the patient had elected revision surgery.

During his 2011 review of the data available from numerous sources, Dr. Carraggee noted the following:

> Comparative review of FDA documents and subsequent publications revealed originally unpublished adverse events and internal inconsistencies. From this review, we suggest an estimate of adverse events associated with rhBMP-2 use in spine fusion ranging from 10% to 50% depending on approach. Posterior lumbar interbody fusion use was associated with radiculitis, ectopic bone formation, osteolysis, and poorer global outcomes.

(*Exhibit 2* at 471-472).

As Dr. Carragee pointed out in his article, between the years 2000 through 2009, "[t]here were 13 original industry-sponsored rhBMP-2 publications regarding safety and efficacy, including reports and analyses of 780 patients receiving rhBMP-2 within prospective controlled study protocols. No rhBMP-2- associated adverse events (0%) were reported in any of these studies (99% confidence interval of adverse event rate <0.5%)." *Id.* at 471.

A copy of Dr. Carragee's notations on those thirteen articles and the estimated amount of money Medtronic paid the authors who wrote those favorable reviews of the product is attached hereto as *Exhibit 4*.

One of the articles was a 2004 piece[1] reviewing the use of BMP for posterior lumbar interbody fusion, an off-label application. It purported to support the safety of BMP in surgeries other than those which fell within the scope of the FDA premarket approval. The article was allegedly based on a prospective nonblinded study in which 67 patients were randomly assigned to one of two groups who underwent interbody fusion using two cylindrical threaded fusion cages: the investigational group (34 patients), who received rhBMP-2 on an absorbable collagen

[1] Haid RW, Branch CL, Alexander JT, Burkus JK. Posterior lumbar interbody fusion using recombinant human bone morphogenetic protein type 2 with cylindrical interbody cages. Spine J 2004;4:527- 38.

sponge, and a control group (33 patients), who received autogenous iliac crest bone graft. It concluded that:

> This small multicenter, randomized, nonblinded trial showed few statistically significant differences between the study groups. Both groups showed comparable improvements on outcome scores. Overall results show that the use of rhBMP-2 can eliminate the need for harvesting iliac crest graft and may be an equivalent replacement for autograft for use in successful posterior lumbar interbody fusions. Further studies of the use of rhBMP-2 in posterior lumbar interbody fusion cage procedures are needed.

Id.

The authors dismissed the development of ectopic bone growth as of no clinical significance to the patients, and failed to mention that with respect to the trials of the 34 patients in the investigational group, that trial was discontinued because of the heterotopic bone growth. The authors had been paid a total of $5,844,000 for what was described by others as a Medtronic marketing piece.

Dr. Carragee's analysis of the risks of clinically significant heterotopic bone growth commenced:

> To avoid the methodological error of analyzing all possible adverse event associations, we confined the comparison of adverse events to those prospectively determined—given the known biology and pharmacology of the rhBMP-2 compound—as being suspect adverse effects before any large trial was reported. As reported by Poynton and Lane in 2002, these were the primary areas of concern:
>
> 1. As reported by Poynton and Lane in 2002, the primary areas of concern included overgrowth bone formation
>
> ....
>
> While Haid et al. reported an incomplete industry-sponsored RCT comparing PLIF using rhBMP-2 with an ICBG control Carragee et al observed that Haid and co-authors also reported, 'no unanticipated device-related adverse events occurred.' They also reported that no patient required reoperation because of an rhBMP-2 adverse event. They concluded that the study 'confirmed the safety' of rhBMP-2 and suggested that the findings might 'eliminate the need' for autograft for 'successful PLIF.' With this presumption of safety, based on 34

study subjects, PLIF and TLIF rapidly became a popular use of rhBMP-2 in the United States: in 2007, 40% to 50% of PLIF/TLIF procedures used rhBMP. On close review, however, several important observations emerge, which were not part of the authors' conclusions.

....

This trial was peremptorily discontinued because of bony overgrowth at the anulotomy site.This was clearly an unanticipated adverse event. Computed tomography scan evaluation found new bone formation into the spinal canal or neuroforamina in 24 of 32 rhBMP-2 patients (70.1 %; 95% CI: 55.27, 85.91) as compared with four of 31 control patients (12.9%; 95% CI: 11.1, 24.7; NNH5 1.6; p5 .0001). Although the authors stated that these findings were not associated with adverse clinical outcomes, the curtailed study was not powered to rule out that effect and the a greater proportion of BMP-2 treated subject reported that the surgery did not help and/or that they were dissatisfied with the surgery.

....

A surgeon, Dr. David G. Malone of Oklahoma, involved in the FDA study reported to the FDA Public Meeting of 2002 that in the experience of his small group with the rhBMP-2/PLIF trial:

> 'two of the [INFUSE] patients had significant posterior bony over-growth impinging on their nerve roots requiring additional surgery. One patient, who was my patient, required two surgeries to clear excessive bone growth from his spinal canal.'

This observation was documented in the FDA record years before the Haid et al. study had been published, but these complications were not included in the authors' comments on unanticipated adverse events related to rhBMP-2 in PLIF surgery.

It was Dr. Malone's opinion expressed to the FDA 2 years before the Haid et al. publication that 'BMP may lead to excessive bone growth and may cause significant neural impingement if placed in posterior lumbar interbody type of device.' The major adverse events in Dr. Malone's patients resulting in reoperation were not reported in the Haid et al. article.

Shortly after that Haid et al. publication, when off-label use of rhBMP-2 in PLIF surgery had begun, Wong et al. reported on five patients with ectopic bone formation in the spinal canal after either PLIF or TLIF using rhBMP-2. These patients reported neurological complaints, and three patients underwent an extensive and 'difficult' revision surgery. Since then, more reports of serious adverse events associated with rhBMP-2 use in this setting have followed.

(*Exhibit 2* at 474, 480-481).

In summary, what happened to Scott Carmine was predictable and preventable. By 2012, the risk of heterotopic bone growth secondary to the use of BMP was known in the literature recognized and read by spinal surgeons. It was certainly known to and by the operating officers of Medtronic.

There is one special feature of the surgery performed on Scott Carmine which increased the risk of heterotopic bone growth to a greater degree. The surgeon not only used BMP in sponges placed inside of Globus PEEK cages, where the migratory path of the BMP when released from the sponge might be somewhat controlled and contained, the surgeon also placed additional BMP sponges in the intervertebral spaces with morselized bone which was tamped down, and the surgeon recorded taking no precautions to prevent or retard the migration of that BMP into unwanted spaces once the sponges were compressed, such as the locations where the heterotopic bone was found and removed, to the degree possible, by the subsequent operating surgeon, Dr. Adam Crowl.

Counsel for Plaintiff has also provided Dr. Carragee with pleadings from the instant litigation in which it appears that Medtronic is defending this case on the basis that Dr. Poffenbarger used their product in an off-label way in that, *inter alia*, he did not employ the Medtronic LT cage during the procedure. Based upon his experience in the field, Dr. Carragee notes that some 85-95% of all lumbar fusions using BMP in the period in question, including the TLIF procedure employed here, were performed in an off-label manner with the full knowledge and tacit support of Medtronic.

As for Dr. Poffenbarger's role in this matter, he either knew of the risks associated with the use of BMP in these procedures or should have known based upon the 2011 publication of those risks in The Spine Journal's April 2011 lead article on those risks. If he proceeded with

the procedure as recorded with knowledge of those risks, then he deviated from the accepted standard of medical care. If he claims to have had no knowledge of the risks of heterotopic bone formation doing the procedure in the manner in which he did, then his deviation from the standard of medical care shall be first a matter for the jury to determine, that is, whether the jury finds and concludes that he should have known of the risks and not have proceeded with the surgery in that manner.

In addition to his opinion that the Medtronic BMP component in its Infuse product as used here was defective in that it was unreasonably dangerous, Dr. Carragee is expected to further testify based upon his knowledge, and as documented by the Staff of the United States Senate Finance Committee in its June 2011 report in Medtronic's possession, that Medtronic had full knowledge of that defect and sought to withhold or disguise that defect through the placement of company-sponsored articles in medical journals that proclaimed the safety of the product, its superiority to the use of native bone harvested from the patient's iliac crest (or elsewhere), and its freedom from adverse consequences, all of which were false.

In addition to his opinion testimony, Dr. Carragee may offer testimony on the use of rhBMP-2 by spine surgeons as a technique to enhance and/or support fusion of vertebral bodies, and the medical literature with respect to that use, and the changes in that literature over time, as well as testify to the federal regulatory history of the use of rhBMP-2, and the published literature describing clinical trials conducted under the auspices of spine surgeons who received compensation from the Defendant Medtronic, compensation which was sometimes undisclosed, and other times incompletely disclosed, and how the reports of the clinical trials conducted by those with economic ties to Medtronic, and the articles published in medical journals by the spine surgeons under contract to Medtronic, failed to disclose specific risks and hazards

encountered during the clinical trials. Specific to the Carmine matter, the medical literature authored by those under contract to Medtronic failed to disclose that a clinical trial which revealed significant ectopic bone growth associated with the use of rhBMP-2 had been abandoned because the rhBMP2 was causing radiographic evidence of an important adverse event in a statistically significant percentage of patients through the growth of ectopic bone, i.e., the development of bone in unwanted areas of the spine in great quantities, called exuberant bone growth. Patient reported outcomes as indicated above suggested this observed effect was causing injury, sometimes permanent injury or requiring recurrent future surgery, as happened to Scott Carmine.

Dr. Carragee may also rebut the opinions of any experts identified by Defendants as provided in designations, depositions and/or trial. He may further testify regarding any medical literature identified pursuant to Va. Code § 8.01-401.1.

2. Adam Crowl, M.D.
OrthoVirginia
13801 St. Francis Boulevard, Suite 200
Midlothian, Virginia 23114

The above-listed physician is Plaintiff's unretained treating provider from OrthoVirginia, formerly Advanced Orthopaedics. Any testimony he renders will be based upon: (a) the medical care and treatment he rendered to Plaintiff; (b) any consultations with other healthcare providers during the course of that treatment; and (c) his training and experience.

Dr. Crowl would be expected to testify in conformity with the OrthoVirginia/Advanced Orthopaedics records reflecting his care and treatment of Plaintiff, including any reasonably held medical opinions identified therein. He may also testify as to the costs associated with his treatment as reflected in the previously disclosed billing records from OrthoVirginia/Advanced Orthopaedics.

3. Michael Decker, M.D.
Advanced Orthopaedics
13801 St. Francis Boulevard, Suite 200
Midlothian, Virginia 23114

The above-listed physician is Plaintiff's unretained treating provider from Advanced Orthopaedics, now OrthoVirginia. Any testimony he renders will be based upon: (a) the medical care and treatment he rendered to Plaintiff; (b) any consultations with other healthcare providers during the course of that treatment; and (c) his training and experience.

Dr. Decker would be expected to testify in conformity with the Advanced Orthopaedics/OrthoVirginia records reflecting his care and treatment of Plaintiff, including any reasonably held medical opinions identified therein. He may also testify as to the costs associated with his treatment as reflected in the previously disclosed billing records from Advanced Orthopaedics/OrthoVirginia.

4. Jed Vanichkachorn, M.D.
Tuckahoe Orthopaedics
8266 Atlee Road
MOB II, Suite 125
Mechanicsville, Virginia 23116

The above-listed physician is Plaintiff's unretained treating provider from Tuckahoe Orthopaedics. Any testimony he renders will be based upon: (a) the medical care and treatment he rendered to Plaintiff; (b) any consultations with other healthcare providers during the course of that treatment; and (c) his training and experience.

Dr. Vanichkachorn would be expected to testify in conformity with the Tuckahoe Orthopaedics records reflecting his care and treatment of Plaintiff, including any reasonably held medical opinions identified therein. He may also testify as to the costs associated with his treatment as reflected in the billing records from Tuckahoe Orthopaedics attached hereto as Exhibit 5.

5. Sudhir Nagaraja, D.O.
Virginia Integrative Psychiatry
4900 Hood Drive
Fredericksburg, Virginia 22408

The above-listed physician is Plaintiff's unretained treating provider from Virginia Integrative Psychiatry. Any testimony he renders will be based upon: (a) the medical care and treatment he rendered to Plaintiff; (b) any consultations with other healthcare providers during the course of that treatment; and (c) his training and experience.

Dr. Nagaraja would be expected to testify in conformity with the Virginia Integrative Psychiatry records reflecting his care and treatment of Plaintiff, including any reasonably held medical opinions identified therein. He may also testify as to the costs associated with his treatment and in accordance with his bill.

6. Plaintiff reserves the right to have his expert witnesses modify and/or supplement any present opinions and/or add opinions as discovery progresses.

7. Plaintiff reserves the right to introduce trial testimony of any reasonably held opinions and/or commentary provided by Plaintiff's identified expert witnesses during deposition.

8. Plaintiff reserves the right to name additional expert witnesses as discovery progresses.

9. Plaintiff reserves the right to call any expert witness at trial named by Defendants and to name rebuttal expert witnesses as necessary. Plaintiff also reserves the right to have his expert witnesses rebut the opinions of Defendants' experts once disclosed and/or deposed.

10. Plaintiff reserves the right to call any additional treating healthcare providers at trial to testify to the opinions and observations formed while treating Plaintiff and documented in his medical records, including those whom may be subsequently deposed during discovery. To

the extent such providers are deposed, Plaintiff reserves the right to introduce trial testimony of any reasonably held opinions and/or commentary provided by them during deposition

11. This designation and all attachments hereto are provided, *inter alia*, as a supplement to Plaintiff's discovery responses in this matter.

12. All opinions offered by Plaintiff's identified expert witnesses will be expressed to a reasonable degree of certainty.

13. This designation was prepared by Plaintiff's counsel, and, as such, the word usage and sentence structure is that of counsel's and does not purport to be the exact language of the identified expert witnesses. The designation is intended only as a summary of the testimony which each witness is expected to offer pursuant to Virginia Supreme Court Rule 4:1(b)(4)(A)(i).

Respectfully Submitted,

SCOTT T. CARMINE,

By Counsel,

Robert T. Hall (VSB #4826)
Hall & Sethi, PLC
11260 Roger Bacon Drive, Suite 400
Reston, Virginia 20190
(703) 925-9500 (telephone)
(703) 925-9166 (facsimile)
rthall@hallandsethi.com
Counsel for Plaintiff

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on this 28th day of August, 2018, a copy of the foregoing was served via electronic mail and first-class mail to:

Coreen A. Silverman, Esq.
Phylicia A. Preston, Esq.
Hancock, Daniel & Johnson, P.C.
4701 Cox Road, Suite 400
Glen Allen, Virginia 23060
(804) 967-9604
(804) 967-9888 (fax)
csilverman@hdjn.com
ppreston@hancockdaniel.com
Counsel for Glen Jeffrey Poffenbarger, M.D., Mary Washington Healthcare Physicians d/b/a Rappahannock Neurosurgery Associates, and Mary Washington Healthcare

Brent R. Gary, Esq.
Reed Smith, LLP
7900 Tysons One Place, Suite 500
McLean, Virginia 22102
bgary@reedsmith.com
Counsel for Medtronic Sofamar Danek USA, Inc. and Medtronic, Inc.

Robert T. Hall